Express Mail No.: EL 501 636 976 US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Ish-Horowicz et al.

Application No.: To be assigned; Divisional of Application Serial No. 08/981,392, filed December 22, 1997

Group Art Unit: To be assigned

Examiner: To be assigned

Filed: on even date herewith

Attorney Docket No.: 7326-122

For: ANTIBODIES TO VERTEBRATE DELTA PROTEINS AND FRAGMENTS (as amended)

PRELIMINARY AMENDMENT FEE TRANSMITTAL SHEET

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

The fee required to be filed with the accompanying preliminary amendment of even date herewith concerning the above-identified application has been estimated to be $2950.00.

The claim amendment fee has been estimated as shown below:

	(Col. 1)			(Col. 2)		(Col. 3)	SMALL ENTITY			OTHER THAN A SMALL ENTITY	
	CLAIMS REMAINING AFTER AMENDMENT			HIGHEST NO PREVIOUSLY PAID FOR		PRESENT EXTRA	RATE	ADDIT. FEE	OR	RATE	ADDIT. FEE
TOTAL	* 120	MINUS	**	20		100	X 9	$		X 18	$1,800.00
INDEP.	* 14	MINUS	***	3		11	X 40	$		X 80	$880.00
☒ FIRST PRESENTATION OF MULTIPLE DEP. CLAIM							+135	$		+270	$270.00
							TOTAL	$	OR	TOTAL	$2950.00
							ADDIT. FEE	$			

Please charge the required fee to Pennie & Edmonds LLP Deposit Account No. 16-1150. A copy of this sheet is enclosed.

Respectfully submitted,

Date February 15, 2001

S. Leslie Misrock — 18,872 (Reg. No.)

By: Adriane M. Antler — 32,605 (Reg. No.)

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PRELIMINARY AMENDMENT UNDER 37 C.F.R. § 1.115

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Pursuant to 37 C.F.R. § 1.121, kindly enter the following amendments and consider the remarks below in connection with the above-identified patent application. Applicant submits concurrently herewith (a) a Preliminary Amendment Fee Transmittal Sheet; (b) a copy of the claims that will be pending upon entry of this amendment; (c) a Sequence Listing in both paper and computer readable forms pursuant to 37 C.F.R. § 1.821; (d) a Transmittal of Sequence Listing; (e) a Declaration under 37 C.F.R. § 1.68 and M.P.E.P.§ 608.01(p); (f) Exhibit A, a copy of Kozbor et al., 1983, Immunology Today 4:72; (g) Exhibit B, a copy of Kohler and Milstein, 1975, Nature 256:495 and (h) Exhibit C, a copy of Huse et al., 1989, Science 246:1275-1281.

IN THE TITLE

Please amend the title as follows:

On page 1, lines 1-2, delete "NUCLEOTIDE AND PROTEIN SEQUENCES OF VERTEBRATE DELTA GENES AND METHODS BASED THEREON" and insert -- ANTIBODIES TO VERTEBRATE DELTA PROTEINS AND FRAGMENTS-- therefor.

IN THE SPECIFICATION

On page 1, delete lines 4-7, and insert the following:

--The present application is a divisional application of Application Serial No. 08/981,392, filed December 22, 1997, national stage of International Application No. PCT/US96/11178 filed June 28, 1996 (published as WO 97/01571 in English), which claims the benefit of provisional Application Serial No. 60/000,589 filed June 28, 1995, each of which is incorporated by reference herein in its entirety.--

On page 10, line 6, delete "(SEQ ID NO:15)" and insert -- (SEQ ID NOS:15-17) --.

On page 10, line 6, delete "(SEQ ID NO:16)" and insert -- (SEQ ID NO:18) --.

On page 10, line 7, delete "(SEQ ID NO:17)" and insert -- (SEQ ID NOS:19-22) --.

On page 10, line 10, delete "(SEQ ID NO:18)" and insert -- (SEQ ID NO:23) --.

On page 10, line 18, delete "(SEQ ID NO:33)" and insert -- (SEQ ID NO:26) --.

On page 10, line 20, delete "(SEQ ID NO:33)" and insert -- (SEQ ID NO:26) --.

On page 10, line 22, delete "(SEQ ID NO:34)" and insert -- (SEQ ID NOS:27-42) --.

On page 10, line 22, delete "(SEQ ID NO:35)" and insert -- (SEQ ID NOS:43-47) --.

On page 10, line 23, delete "(SEQ ID NO:36)" and insert -- (SEQ ID NOS:48-64) --.

On page 10, line 34, delete "(SEQ ID NO:37)" and insert -- (SEQ ID NO:4) --.

On page 10, line 35, delete "(SEQ ID NO:33)" and insert -- (SEQ ID NO:26) --.

On page 10, line 36, delete "(SEQ ID NO:38)" and insert -- (SEQ ID NO:24) --.

On page 11, line 2, delete "(SEQ ID NOS:39-65)" and insert -- (SEQ ID NOS:65-80) --.

On page 13, line 37, delete "(SEQ ID NO:33)" and insert -- (SEQ ID NO:26) --.

On page 14, line 2, delete "SEQ ID NO:1, 3, 11, 14 or 33" and insert -- SEQ ID NO:1, 3, 11, 14 or 26 --.

On page 14, line 16, delete "SEQ ID NO:33" and insert -- SEQ ID NO:26 --.

On page 26, line 23, delete "(SEQ ID NOS:2, 10, 16 and 39-65)" and insert -- (SEQ ID NOS:2, 12, 23 and 65-80) --.

On page 29, line 26, after "used" insert the following text:

-- Two conceptually unique approaches are currently available for the production of human monoclonal antibodies - the 'hybridoma' technique, based on the fusion of antibody-producing B lymphocytes with plasmacytoma cells or lymphoblastoid cell lines; and the use of Epstein-Barr virus (EBV) to 'immortalize' antigen-specific human B lymphocytes. --

On page 29, line 28, after "Milstein", insert -- (The cell lines are made by fusion of a mouse myeloma and mouse spleen cells from an immunised donor.) --

On page 29, line 33, before "In an", insert the following text:

-- In this technique, as in the hybridoma procedure, it is important to use the blood lymphocytes of individuals who have previously been immunized with the antigens and have increased numbers of specific antibody-producing cells. The procedure involves two steps: (1) the enrichment of cells with receptors for the given antigen; and (2) 'immortalization' of these cells by EBV infection.--

On page 30, line 21, after "analogs.", insert the following text:

-- As reported by Huse et al., an Fab expression library was constructed from mRNA isolated from a mouse that had been immunized with the antigen NPN. The PCR amplification of messenger RNA isolated from spleen cells or hybridomas with oligonucleotides that incorporate restriction sites into the ends of the amplified product can be used to clone and express heavy and light chain sequences. Thus, the amplified fragments were cloned into a lambda phage vector in a predetermined reading frame for expression. The combinatorial library was constructed in two steps. In the first step, separate heavy and light chain libraries were constructed, and in the second step, these two libraries were used to construct a combinatorial library by crossing them at the EcoRI site. After ligation, only clones that resulted from combination of a right arm of light chain-containing clones and a left arm of heavy chain-containing clones reconstituted a viable phage. After ligation and packaging, 2.5

x 10^7 clones were obtained. This is the combinatorial Fab expression library that was screened to identify clones having affinity for NPN. In an examination of approximately 500 recombinant phage, approximately 60 percent coexpressed light and heavy chain proteins. The light chain, heavy chain and Fab libraries were screened to determine whether they contained recombinant phage that expressed antibody fragments binding NPN.--

On page 37, line 20, delete "SEQ ID NO:2 or 16" and insert -- SEQ ID NO:2 or 23 --.

On page 68, line 7, delete "(SEQ ID NO:19)" and insert -- (SEQ ID NO:81) --.

On page 68, line 8, delete "(SEQ ID NO:20)" and insert -- (SEQ ID NO:82) --.

On page 68, line 9, delete "(SEQ ID NO:21)" and insert -- (SEQ ID NO:83) --.

On page 68, line 10, delete "(SEQ ID NO:22)" and insert -- (SEQ ID NO:84) --.

On page 68, line 31, after "...LGV)" insert the phrase -- (SEQ ID NO:85) --.

On page 75, line 4, delete "(SEQ ID NO:23)" and insert -- (SEQ ID NO:86) --.

On page 75, line 4, delete "(SEQ ID NO:24)" and insert -- (SEQ ID NO:94) --.

On page 75, line 9, delete "(SEQ ID NO:25)" and insert -- (SEQ ID NO:87) --.

On page 75, line 9, delete "(SEQ ID NO:26)" and insert -- (SEQ ID NO:88) --.

On page 76, line 12, delete "(SEQ ID NO:27)" and insert -- (SEQ ID NO:89) --.

On page 76, line 13, delete "(SEQ ID NO:28)" and insert -- (SEQ ID NO:90) --.

On page 76, line 14, delete "(SEQ ID NO:29)" and insert -- (SEQ ID NO:91) --.

On page 76, line 15, delete "(SEQ ID NO:30)" and insert -- (SEQ ID NO:92) --.

On page 76, line 17, delete "(SEQ ID NO:31)" and insert -- (SEQ ID NO:93) --.

On page 76, line 17, delete "(SEQ ID NO:32)" and insert -- (SEQ ID NO:25) --.

On page 76, line 27, delete "(SEQ ID NOS:15,16,17)" and insert -- (SEQ ID NOS:15-22) --.

On page 76, line 33, delete "(SEQ ID NO:18)" and insert -- (SEQ ID NO:23) --.

On page 78, line 5, delete "(SEQ ID NO:33)" and insert -- (SEQ ID NO:26) --.

On page 78, line 8, delete "(SEQ ID NO:33)" and insert -- (SEQ ID NO:26) --.

On page 78, line 11, delete "(SEQ ID NO:34)" and insert -- (SEQ ID NOS:27-42) --.

On page 78, line 12, delete "(SEQ ID NO:35)" and insert -- (SEQ ID NOS:43-47) --.

On page 78, line 13, delete "(SEQ ID NO:36)" and insert -- (SEQ ID NOS:48-64) --.

On page 78, line 21, delete "(SEQ ID NOS:39 through 65.)" and insert -- (SEQ ID NOS:65-80) --.

On page 78, line 32, delete "(SEQ ID NO:37)" and insert -- (SEQ ID NO:4) --.

On page 78, line 34, delete "(SEQ ID NO:33)" and insert -- (SEQ ID NO:26) --.

On page 78, line 36, delete "(SEQ ID NO:38)" and insert -- (SEQ ID NO:24) --.

After the Figures, insert pages 1-51 of the Sequence Listing submitted herewith.

IN THE CLAIMS:

Please amend the claims as follows:

29 (once amended). An antibody which [is capable of binding the Delta protein of claim 1] binds a vertebrate Delta protein, which Delta protein is encoded by a first

nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS, and which antibody does not bind [to] a *Drosophila* Delta protein.

30 (once amended). An antibody, which [is capable of binding the Delta protein of claim 2, and] binds a human Delta protein, which Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, and the antisense strand to the human *Delta* sequence of SEQ ID NO:26, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution

containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS, which does not bind [to] a *Drosophila* Delta protein.

31 (once amended). The antibody of claim [1] 29 or 30 which is monoclonal.

32 (once amended). A molecule comprising a fragment of the antibody of claim 31, which fragment [is capable of binding] binds a vertebrate Delta protein.

60 (once amended). A [pharmaceutical] composition comprising [a therapeutically effective] an amount of an antibody which binds to a vertebrate Delta protein; and a pharmaceutically acceptable carrier, which Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS, and which antibody does not bind a *Drosophila* Delta protein.

61 (once amended). A [pharmaceutical] composition comprising [a therapeutically effective] an amount of a fragment or derivative of an antibody to a vertebrate Delta protein containing the binding domain of the antibody; and a pharmaceutically acceptable carrier, which Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the

antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS, and which antibody does not bind a *Drosophila* Delta protein.

Please add the following new claims:

99 (new). The antibody of claim 29, 60 or 61, in which the Delta protein comprises an amino acid sequence selected from the group consisting of the chick Delta sequence of SEQ ID NO:2, the mouse Delta sequence of SEQ ID NO:12, the human Delta sequence of SEQ ID NO:23, and the human Delta sequence of SEQ ID NOS:65-80.

100 (new). The composition of claim 60 or 61, in which the antibody is monoclonal.

101 (new). A fragment of the antibody of claim 29 or 30, which fragment binds a vertebrate Delta protein.

102 (new). The antibody of claim 29, 30, 31 or 99, which antibody is purified.

103 (new). The fragment of claim 101, which fragment is purified.

104 (new). The molecule of claim 32, which molecule is purified.

105 (new). The antibody of claim 29, in which the Delta protein comprises the amino acid sequence of SEQ ID NOS:65-80.

106 (new). The antibody of claim 29, in which the Delta protein comprises the amino acid sequence of SEQ ID NO:23.

107 (new). The antibody of claim 29, in which the Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, and the antisense strand to the human *Delta* sequence of SEQ ID NO:26, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS.

108 (new). The antibody of claim 29, in which the Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS.

109 (new). A method of making an antibody comprising:

(a) administering an immunogenic amount of a vertebrate Delta protein to a host animal, in which the Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the

antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS, such that an antibody to said Delta protein is produced by said host animal; and

(b) recovering the antibody.

110 (new). The method of claim 109, in which the Delta protein comprises the amino acid sequence of SEQ ID NOS:65-80.

111 (new). The method of claim 109, in which the Delta protein comprises the amino acid sequence of SEQ ID NO:23.

112 (new). The method of claim 109, in which the Delta protein comprises the amino acid sequence of SEQ ID NO:12.

113 (new). The method of claim 109, in which the Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, and the antisense strand to the human *Delta* sequence of SEQ ID NO:26, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution

containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS.

114 (new). A method of making an antibody comprising:

(a) administering an immunogenic amount of a fragment of a vertebrate Delta protein to a host animal, in which the fragment comprises a domain of the protein selected from the group consisting of the extracellular domain, DSL domain, domain amino-terminal to the DSL domain, epidermal growth factor-like repeat domain, transmembrane domain, and intracellular domain, in which the Delta protein is comprises an amino acid sequence encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS, such that an antibody to said fragment is produced by said host animal; and

(b) recovering the antibody.

115 (new). The method of claim 114, in which the fragment of the vertebrate Delta protein comprises the membrane-associated region of the Delta protein.

116 (new). The method of claim 114, in which the fragment of the vertebrate Delta protein comprises an epidermal growth factor-homologous repeat of the protein.

117 (new). The method of claim 114, in which the fragment of the vertebrate Delta protein consists of at least 20 contiguous amino acids of the vertebrate Delta protein.

118 (new). The method of claim 114, in which the fragment of the vertebrate Delta protein lacks the transmembrane and intracellular domain of the protein.

119 (new). The method of claim 114, in which the fragment of the vertebrate Delta protein lacks the extracellular domain of the protein.

120 (new). The method of claim 114, in which the fragment of the vertebrate Delta protein lacks the epidermal growth factor-like repeats of the protein.

121 (new). An antibody produced by the method of claim 109, which does not bind a *Drosophila* Delta protein.

122 (new). An antibody produced by the method of claim 114, which does not bind a *Drosophila* Delta protein.

123 (new). The antibody of claim 121 or 122, in which the antibody is monoclonal.

124 (new). The antibody of claim 121, 122 or 123, in which the antibody is purified.

125 (new). A composition comprising an amount of an antibody of claim 121, 122, 123 or 124, and a pharmaceutically acceptable carrier.

126 (new). The method of claim 109 or 114, in which the Delta protein comprises an amino acid sequence selected from the group consisting of the chick Delta sequence of SEQ ID NO:2, the mouse Delta sequence of SEQ ID NO:12, the human Delta sequence of SEQ ID NO:23, and the human Delta sequence of SEQ ID NOS:65-80.

127 (new). The method of claim 109 or 114, in which the Delta protein comprises an amino acid sequence selected from the group consisting of the human Delta sequence of SEQ ID NO:23.

128 (new). The method of claim 109 or 114, in which the Delta protein comprises an amino acid sequence selected from the group consisting of the human Delta sequence of SEQ ID NOS:65-80.

129 (new). A method of making an antibody comprising:

(a) administering an immunogenic amount of a protein comprising a fragment of a vertebrate Delta protein to a host animal, in which the fragment comprises a domain of the

protein selected from the group consisting of the extracellular domain, DSL domain, domain amino-terminal to the DSL domain, epidermal growth factor-like repeat domain, transmembrane domain, and intracellular domain, in which the Delta protein is comprises an amino acid sequence encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS, such that an antibody to said Delta fragment is produced by said host animal; and

(b) recovering the antibody.

130 (new). The method according to claim 129, in which the fragment of the Delta protein is joined via a peptide bond to an amino acid sequence of a second protein, in which the second protein is not the Delta protein.

131 (new). A method of making a monoclonal antibody comprising:

(a) administering an immunogenic amount of a vertebrate Delta protein to a mouse, in which the Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the

antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 μg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 μg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS;

(b) recovering spleen cells from said mouse;

(c) fusing the recovered spleen cells with a cell of a mouse myeloma to generate hybridomas;

(d) screening to select a hybridoma producing antibody to said vertebrate Delta protein; and

(e) recovering the antibody.

132 (new). A method of making a monoclonal antibody comprising:

(a) fusing a spleen cell from a mouse immunized with an immunogenic amount of a vertebrate Delta protein with a cell of a mouse myeloma to generate hybridomas, in which the Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of

SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS;

(b) screening to select a hybridoma producing antibody to said vertebrate Delta protein; and

(c) recovering the antibody.

133 (new). A method of making a monoclonal antibody comprising:

(a) administering an immunogenic amount of a vertebrate Delta protein to a host animal, in which the Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5

mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS;

(b) recovering lymphocytes from said host animal;

(c) fusing the recovered lymphocytes with a cell of a myeloma, plastocytoma or lymphoblastoid cell line to generate hybridomas;

(d) screening to select a hybridoma producing antibody to said vertebrate Delta protein; and

(e) recovering the antibody.

134 (new). A method of making a monoclonal antibody comprising:

(a) fusing a lymphocyte from a host animal immunized with an immunogenic amount of a vertebrate Delta protein with a cell of a myeloma, plastocytoma or lymphoblastoid cell line to generate hybridomas, in which the Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS;

(b) screening to select a hybridoma producing antibody to said vertebrate Delta protein; and

(c) recovering the antibody.

135 (new). A method of making a monoclonal antibody comprising:

(a) administering an immunogenic amount of a vertebrate Delta protein to a host animal, in which the Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS;

(b) recovering lymphocytes from said host animal;

(c) immortalizing the recovered lymphocytes with Epstein-Barr virus to generate immortalized cells;

(d) screening to select an immortalized cell producing antibody to said vertebrate Delta protein; and

(e) recovering the antibody.

136 (new). A method of making a monoclonal antibody comprising:

(a) immortalizing a lymphocyte from a host animal immunized with an immunogenic amount of a vertebrate Delta protein with Epstein-Barr virus to generate immortalized cells, in which the Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the

antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS;

(b) screening to select an immortalized cell producing antibody to said vertebrate Delta protein; and

(c) recovering the antibody.

137 (new). A method of producing a phage Fab expression library comprising:

(a) isolating spleen cells from a host animal immunized with an immunogenic amount of a vertebrate Delta protein, in which the Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions

comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS;

(b) amplifying, by polymerase chain reaction, antibody heavy and light chain nucleotide sequences from messenger RNA isolated from the spleen cells;

(c) cloning the amplified heavy chain and light chain nucleotide sequences into a lambda phage vector to produce a heavy chain library and a light chain library, respectively;

(d) combining and ligating the heavy and light chain nucleotide sequences from the heavy chain and light chain libraries to produce a phage Fab expression library that co-expresses antibody heavy and light chains; and

(e) screening the expression library for a phage that binds said Delta protein.

138 (new). The method of claim 131, 132, 133, 134, 135, 136 or 137, which second nucleic acid is selected from the group consisting of the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24.

139 (new). The method of claim 131, 132, 133, 134, 135, 136 or 137, in which the Delta protein comprises the amino acid sequence of SEQ ID NOS:65-80.

140 (new). The method of claim 131, 132, 133, 134, 135, 136 or 137, in which the Delta protein comprises the amino acid sequence of SEQ ID NO:23.

141 (new). The method of claim 131, 132, 133, 134, 135, 136 or 137, in which the Delta protein comprises the amino acid sequence of SEQ ID NO:12.

142 (new). An antibody produced by the method of claim 131, 132, 133, 134, 135, 136 or 137, which does not bind a *Drosophila* Delta protein.

143 (new). The antibody of claim 142, in which the antibody is purified.

144 (new). A composition comprising the antibody of claim 142, and a pharmaceutically acceptable carrier.

145 (new). A composition comprising the antibody of claim 143, and a pharmaceutically acceptable carrier.

REMARKS

The title has been amended to recite "ANTIBODIES TO VERTEBRATE DELTA PROTEINS AND FRAGMENTS" such that the title is clearly indicative of the claimed subject matter.

The specification has been amended to reflect that the present application is a divisional application of Application Serial No. 08/981,392, filed December 22, 1997. The specification has also been amended to incorporate the correct sequence identifiers pursuant to 37 C.F.R. § 1.821(d) and the Sequence Listing submitted herewith pursuant to 37 C.F.R. § 1.821(c).

The specification has been amended at page 29, lines 26, 28 and 33, and at page 30, line 21 to insert the same material as that incorporated by reference, in accordance with M.P.E.P 2163.07(b) and 608.01(p). No new matter has been introduced. Specifically, Kozbor et al., 1983, Immunology Today 4:72 (a copy of which is attached hereto as Exhibit A) was incorporated by reference at page 29, lines 26 and 33 of the specification with respect to the description, at page 29, lines 23-30, for types of production of antibody molecules by continuous cell lines. The actual text of the first sentence of the Abstract at page 72, and the actual text of the first two sentences of the section entitled *Selection of antigen-specific cells* on page 76, left column have been inserted into the specification. Additionally, Kohler and Milstein, 1975, Nature 256:495 (a copy of which is attached hereto as Exhibit B) was incorporated by reference at page 29, line 28 of the specification with respect to the description, at page 29, lines 23-30, for types of production of antibody molecules by continuous cell lines. The actual text of a sentence on page 495, left column, has been inserted into the specification. Further, Huse et al., 1989, Science 246:1275-1281 (a copy of which is attached hereto as Exhibit C) was incorporated by reference at page 30, line 21 of the specification with respect to the description, at page 30, lines 13-21, for the production of phage Fab expression libraries. The same subject matter as in the text from page 1277, left column, to page 1278, right column, has been inserted into the specification.

Applicants submit herewith a Declaration under 37 C.F.R. § 1.68 and M.P.E.P. 608.01(p) which states that the amendatory material that was included in the specification at page 29, lines 26, 28 and 33 consists of the same material incorporated by

reference in the application as filed at page 29, lines 23-30, and that the amendatory material that was included in the specification at page 30, line 21 consists of the same material incorporated by reference in the application as filed at page 30, lines 13-21.

Upon entry of this amendment, claims 29-32, 60, 61 and 99-145 will be pending. Claims 29-32, 60 and 61 have been amended, and new claims 99-145 have been added, to more particularly point out and distinctly claim the subject matter of the present invention. Specifically, claims 29, 60 and 61 have been amended to recite that the antibody binds a vertebrate Delta protein, which Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS, and which antibody does not bind a *Drosophila* Delta protein. Support for this amendment is found in the specification as filed, *inter alia*, at page 12, lines 14-15; page 13, line 33 to page 15, line 3; page 28, line 31 to page 29, line 4; page 30, line 22 to page 31, line 3; and Figures 1, 7, 10 and 12.

Claim 30 has been made independent and recites an antibody, which binds a human Delta protein, which Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second

nucleic acid is selected from the group consisting of the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, and the antisense strand to the human *Delta* sequence of SEQ ID NO:26, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS, which does not bind a *Drosophila* Delta protein. Support for this amendment is found in the specification as filed, *inter alia*, at page 12, lines 14-15; page 13, line 33 to page 15, line 3; page 28, line 31 to page 29, line 4; page 30, line 22 to page 31, line 3; and Figures 10 and 12. Claim 31 has been amended to depend from claim 29 or 30. Claim 32 has been amended to recite that the fragment of the antibody binds a vertebrate Delta protein. Support for this claim is found in the specification at page 28, lines 31-34.

New claims 99-145 have been added. Support for the newly added claims is set forth in the table below.

CLAIM	SUPPORT IN THE SPECIFICATION
99, 126	page 25, line 8 to page 26, line 24; Figures 2, 8, 11 and 14
100, 123	page 29, lines 23-26
101	page 30, lines 22-30
102-104, 124, 143	page 31, lines 13-15; page 60, lines 19-20; page 64, lines 15-18
109, 114, 129	page 12, lines 14-15, page 13, line 33 to page 15, line 3; page 28, line 31 to page 31, line 15; Figures 1, 7, 10 and 12
105, 110, 128, 139	page 12, lines 14-15, page 13, line 33 to page 15, line 3; page 28, line 31 to page 31, line 15; Figure 14; Section 8 (pages 76-70)

106, 111, 127, 140	page 12, lines 14-15, page 13, line 33 to page 15, line 3; page 28, line 31 to page 31, line 15; Figure 10; Section 8 (pages 76-79)
107, 108, 113, 138	page 13, line 33 to page 15, line 3, Figures 10, 12
112, 141	page 12, lines 14-15, page 13, line 33 to page 15, line 3; page 28, line 31 to page 31, line 15; Figure 7; Section 7 (pages 74-75)
115, 116, 118-120	page 25, lines 24-32; page 30, lines 33-37; page 36, line 24 to page 37, line 23
117	page 33, lines 11-33
121, 122, 142	page 28, line 31 to page 31, line 15
125, 144, 145	page 31, lines 13-15; page 63, line 18 to page 64, line 18
130	page 35, lines 6-12
131-137	page 12, lines 14-15, page 13, line 33 to page 15, line 3; page 28, line 31 to page 31, line 15; Figures 1, 7, 10 and 12; and in the text that was inserted at page 26, lines 26, 29 and 33 and at page 30, line 21 by amendment herein

None of the above-made amendments constitute new matter under 35 U.S.C. § 132.

CONCLUSION

Applicants respectfully request that the above-made amendments and remarks of the present preliminary amendment be entered and made of record in the file history of this application.

Respectfully submitted,

Date: February 15, 2001

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CLAIMS THAT WILL BE PENDING UPON ENTRY OF PRELIMINARY AMENDMENT

29. An antibody which binds a vertebrate Delta protein, which Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS, and which antibody does not bind a *Drosophila* Delta protein.

30. An antibody, which binds a human Delta protein, which Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, and the antisense strand to the human *Delta* sequence of SEQ ID NO:26, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC,

50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS, which does not bind a *Drosophila* Delta protein.

31. The antibody of claim 29 or 30 which is monoclonal.

32. A molecule comprising a fragment of the antibody of claim 31, which fragment binds a vertebrate Delta protein.

60. A composition comprising an amount of an antibody which binds to a vertebrate Delta protein; and a pharmaceutically acceptable carrier, which Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a

second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS, and which antibody does not bind a *Drosophila* Delta protein.

61. A composition comprising an amount of a fragment or derivative of an antibody to a vertebrate Delta protein containing the binding domain of the antibody; and a pharmaceutically acceptable carrier, which Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS, and which antibody does not bind a *Drosophila* Delta protein.

Please add the following new claims:

99. The antibody of claim 29, 60 or 61, in which the Delta protein comprises an amino acid sequence selected from the group consisting of the chick Delta sequence of SEQ ID NO:2, the mouse Delta sequence of SEQ ID NO:12, the human Delta sequence of SEQ ID NO:23, and the human Delta sequence of SEQ ID NOS:65-80.

100. The composition of claim 60 or 61, in which the antibody is monoclonal.

101. A fragment of the antibody of claim 29 or 30, which fragment binds a vertebrate Delta protein.

102. The antibody of claim 29, 30, 31 or 99, which antibody is purified.

103. The fragment of claim 101, which fragment is purified.

104. The molecule of claim 32, which molecule is purified.

105. The antibody of claim 29, in which the Delta protein comprises the amino acid sequence of SEQ ID NOS:65-80.

106. The antibody of claim 29, in which the Delta protein comprises the amino acid sequence of SEQ ID NO:23.

107. The antibody of claim 29, in which the Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, and the antisense strand to the human *Delta* sequence of SEQ ID NO:26, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS.

108. The antibody of claim 29, in which the Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon

sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS.

109. A method of making an antibody comprising:

(a) administering an immunogenic amount of a vertebrate Delta protein to a host animal, in which the Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS, such that an antibody to said Delta protein is produced by said host animal; and

(b) recovering the antibody.

110. The method of claim 109, in which the Delta protein comprises the amino acid sequence of SEQ ID NOS:65-80.

111. The method of claim 109, in which the Delta protein comprises the amino acid sequence of SEQ ID NO:23.

112. The method of claim 109, in which the Delta protein comprises the amino acid sequence of SEQ ID NO:12.

113. The method of claim 109, in which the Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, and the antisense strand to the human *Delta* sequence of SEQ ID NO:26, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS.

114. A method of making an antibody comprising:

(a) administering an immunogenic amount of a fragment of a vertebrate Delta protein to a host animal, in which the fragment comprises a domain of the protein selected from the group consisting of the extracellular domain, DSL domain, domain amino-terminal to the DSL domain, epidermal growth factor-like repeat domain, transmembrane domain, and intracellular domain, in which the Delta protein is comprises an amino acid sequence encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human

Delta sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 μg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 μg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS, such that an antibody to said fragment is produced by said host animal; and

(b) recovering the antibody.

115. The method of claim 114, in which the fragment of the vertebrate Delta protein comprises the membrane-associated region of the Delta protein.

116. The method of claim 114, in which the fragment of the vertebrate Delta protein comprises an epidermal growth factor-homologous repeat of the protein.

117. The method of claim 114, in which the fragment of the vertebrate Delta protein consists of at least 20 contiguous amino acids of the vertebrate Delta protein.

118. The method of claim 114, in which the fragment of the vertebrate Delta protein lacks the transmembrane and intracellular domain of the protein.

119. The method of claim 114, in which the fragment of the vertebrate Delta protein lacks the extracellular domain of the protein.

120. The method of claim 114, in which the fragment of the vertebrate Delta protein lacks the epidermal growth factor-like repeats of the protein.

121. An antibody produced by the method of claim 109, which does not bind a *Drosophila* Delta protein.

122. An antibody produced by the method of claim 114, which does not bind a *Drosophila* Delta protein.

123. The antibody of claim 121 or 122, in which the antibody is monoclonal.

124. The antibody of claim 121, 122 or 123, in which the antibody is purified.

125. A composition comprising an amount of an antibody of claim 121, 122, 123 or 124, and a pharmaceutically acceptable carrier.

126. The method of claim 109 or 114, in which the Delta protein comprises an amino acid sequence selected from the group consisting of the chick Delta sequence of SEQ ID NO:2, the mouse Delta sequence of SEQ ID NO:12, the human Delta sequence of SEQ ID NO:23, and the human Delta sequence of SEQ ID NOS:65-80.

127. The method of claim 109 or 114, in which the Delta protein comprises an amino acid sequence selected from the group consisting of the human Delta sequence of SEQ ID NO:23.

128. The method of claim 109 or 114, in which the Delta protein comprises an amino acid sequence selected from the group consisting of the human Delta sequence of SEQ ID NOS:65-80.

129. A method of making an antibody comprising:

(a) administering an immunogenic amount of a protein comprising a fragment of a vertebrate Delta protein to a host animal, in which the fragment comprises a domain of the protein selected from the group consisting of the extracellular domain, DSL domain, domain amino-terminal to the DSL domain, epidermal growth factor-like repeat domain, transmembrane domain, and intracellular domain, in which the Delta protein is comprises an amino acid sequence encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency

conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS, such that an antibody to said Delta fragment is produced by said host animal; and

(b) recovering the antibody.

130. The method according to claim 129, in which the fragment of the Delta protein is joined via a peptide bond to an amino acid sequence of a second protein, in which the second protein is not the Delta protein.

131. A method of making a monoclonal antibody comprising:

(a) administering an immunogenic amount of a vertebrate Delta protein to a mouse, in which the Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.)

dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS;

(b) recovering spleen cells from said mouse;

(c) fusing the recovered spleen cells with a cell of a mouse myeloma to generate hybridomas;

(d) screening to select a hybridoma producing antibody to said vertebrate Delta protein; and

(e) recovering the antibody.

132. A method of making a monoclonal antibody comprising:

(a) fusing a spleen cell from a mouse immunized with an immunogenic amount of a vertebrate Delta protein with a cell of a mouse myeloma to generate hybridomas, in which the Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS;

(b) screening to select a hybridoma producing antibody to said vertebrate Delta protein; and

(c) recovering the antibody.

133. A method of making a monoclonal antibody comprising:

(a) administering an immunogenic amount of a vertebrate Delta protein to a host animal, in which the Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS;

(b) recovering lymphocytes from said host animal;

(c) fusing the recovered lymphocytes with a cell of a myeloma, plastocytoma or lymphoblastoid cell line to generate hybridomas;

(d) screening to select a hybridoma producing antibody to said vertebrate Delta protein; and

(e) recovering the antibody.

134. A method of making a monoclonal antibody comprising:

(a) fusing a lymphocyte from a host animal immunized with an immunogenic amount of a vertebrate Delta protein with a cell of a myeloma, plastocytoma or lymphoblastoid cell line to generate hybridomas, in which the Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS;

(b) screening to select a hybridoma producing antibody to said vertebrate Delta protein; and

(c) recovering the antibody.

135. A method of making a monoclonal antibody comprising:

(a) administering an immunogenic amount of a vertebrate Delta protein to a host animal, in which the Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the

antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS;

(b) recovering lymphocytes from said host animal;

(c) immortalizing the recovered lymphocytes with Epstein-Barr virus to generate immortalized cells;

(d) screening to select an immortalized cell producing antibody to said vertebrate Delta protein; and

(e) recovering the antibody.

136. A method of making a monoclonal antibody comprising:

(a) immortalizing a lymphocyte from a host animal immunized with an immunogenic amount of a vertebrate Delta protein with Epstein-Barr virus to generate immortalized cells, in which the Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID

NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS;

(b) screening to select an immortalized cell producing antibody to said vertebrate Delta protein; and

(c) recovering the antibody.

137. A method of producing a phage Fab expression library comprising:

(a) isolating spleen cells from a host animal immunized with an immunogenic amount of a vertebrate Delta protein, in which the Delta protein is encoded by a first nucleic acid that hybridizes under low stringency conditions to a second nucleic acid, or its complement, which second nucleic acid is selected from the group consisting of the chick *Delta* sequence of SEQ ID NO:1, the antisense strand to the chick *Delta* sequence of SEQ ID NO:1, the chick *Delta* sequence of SEQ ID NO:3, the antisense strand to the chick *Delta* sequence of SEQ ID NO:3, the mouse *Delta* sequence of SEQ ID NO:11, the antisense strand to the mouse *Delta* sequence of SEQ ID NO:11, the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24, said low stringency conditions comprising pretreatment for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 18-20 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM

Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 μg/ml denatured salmon sperm DNA, and 10% (wt./vol.) dextran sulfate; washing for 1.5 hours at 55°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS; and a second washing for 1.5 hours at 60°C in a solution containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA and 0.1% SDS;

(b) amplifying, by polymerase chain reaction, antibody heavy and light chain nucleotide sequences from messenger RNA isolated from the spleen cells;

(c) cloning the amplified heavy chain and light chain nucleotide sequences into a lambda phage vector to produce a heavy chain library and a light chain library, respectively;

(d) combining and ligating the heavy and light chain nucleotide sequences from the heavy chain and light chain libraries to produce a phage Fab expression library that co-expresses antibody heavy and light chains; and

(e) screening the expression library for a phage that binds said Delta protein.

138. The method of claim 131, 132, 133, 134, 135, 136 or 137, which second nucleic acid is selected from the group consisting of the human *Delta* sequence of SEQ ID NO:14, the antisense strand to the human *Delta* sequence of SEQ ID NO:14, the human *Delta* sequence of SEQ ID NO:26, the antisense strand to the human *Delta* sequence of SEQ ID NO:26, the mouse-human *Delta* consensus sequence of SEQ ID NO:24, and the antisense strand to the mouse-human *Delta* consensus sequence of SEQ ID NO:24.

139. The method of claim 131, 132, 133, 134, 135, 136 or 137, in which the Delta protein comprises the amino acid sequence of SEQ ID NOS:65-80.

140. The method of claim 131, 132, 133, 134, 135, 136 or 137, in which the Delta protein comprises the amino acid sequence of SEQ ID NO:23.

141. The method of claim 131, 132, 133, 134, 135, 136 or 137, in which the Delta protein comprises the amino acid sequence of SEQ ID NO:12.

142. An antibody produced by the method of claim 131, 132, 133, 134, 135, 136 or 137, which does not bind a *Drosophila* Delta protein.

143. The antibody of claim 142, in which the antibody is purified.

144. A composition comprising the antibody of claim 142, and a pharmaceutically acceptable carrier.

145. A composition comprising the antibody of claim 143, and a pharmaceutically acceptable carrier.